"Development of Green Methodologies and its Applicationin Synthesis of Organic Compounds"

RESEARCH PROPOSAL SUBMITTED TO

Swami Ramanand Teerth MarathwadaUniversity, Nanded

FOR AWARD OF DEGREE

DOCTOR OF PHILOSOPHY (Ph.D.) IN THE

FACULTY OF SCIENCE **SUBJECT:**

CHEMISTRY

SUBMITTED BY

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Proposed Research Work Plan

Title: Development of Green Methodologies and its Application in Synthesis of Organic Compounds.

1. Introduction:

Sustainability means 'meeting the needs of the present generation without compromising the needs of future generations. To reach this sustainable development each and everything around the glove are changing rapidly and chemistry is not the exception. Among the various changes and modifications in this subject the keen success has been achieved towards the synthesis of new product and process as the twelve principles of "Green Chemistry" was formulated in 1990s.1 We the chemists both as academia or industry are trying our level best to follow the twelve principles while doing chemical reactions. If we go through all these twelve principles of green chemistry it will be seen that the motto of all the principles is same. Thus, keeping all respects in the twelve principles of green chemistry we can express these as 12 D's. Solvent-less technology has a number of advantages from the viewpoint of both academy and industry. Two of twelve principles of "Green Chemistry" are to "use of safer solvent and reactions condition" and to "prevent waste". These principles are both directly met by eliminating a reaction medium. Solvent-free and/or solvent-less protocol frequently display remarkable rate acceleration due to the increased reaction conditions with some occurring under ambient situation i.e., at room temperature, microwave irradiation, ball milling. The poisonous and volatile nature of many organic solvents particularly chlorinated hydrocarbon that are commonly used in huge amounts for organic reaction have created a serious warning to the human health and environment. Thus, propose of solvent-less catalytic reaction has gained undisputed attention in recent times in the area of green synthesis.

2. Literature Survey:

Three common widespread synthetic strategies have been reported for the synthesis of 2-aryl benzothiazoles. The first most common strategy for synthesis of 2-arylbenzothiazoles is condensation of 2-aminothiophenol with carbonyl compounds such as aldehydes, β-diketones, aryl ketones, carboxylic acids, amides, acyl halides, β-ketoesters, β-ketonitriles and α-ketoacids. The second common approach reported for construction of 2-arylbenzthiazole was cross- coupling and C-H functionalization processes by using various catalytic systems. Third effective strategy has been demonstrated for construction of 2-arylbenzothiazoles was oxidative intramolecular cyclization of thiobenzanilides.

The number of methods has been developed for the synthesis of 1-amidoalkyl-2- naphthols scaffolds by using different Lewis or Brönsted acid catalysts, heterogeneous organic and inorganic catalysts, deep eutectic solvents and ionic liquids. The reported methods used for preparation of 1-amidoalkyl-2-naphthols include the catalysts such as p-TSA, $Fe(HSO_4)_3$, P_2O_5, I_2, VB_1, $HClO_4$-SiO_2, wet-TCT, $ZrO(OTf)_2$, $Bi(NO_3)_3$, zwitterionic salts, sulphamic acid, DPA, graphine oxide, MSNs-HPZ-SO_3H**,** β-CD-BSA, $NiFe_2O_4$@SiO_2-PPA, carbon-SO_3H, $Bi(OTf)_3$, $InCl_3$, $Cu(OTf)_2$.SiO_2, SiO_2-$NaHSO_4$, MoO_3-ZrO_2, nano-Fe_3O_4-SO_3H, Cellulose-SO_3H, $H_4SiW_{12}O_{40}$, MCM-41-N-propylsufamic acid, $FeCl_3$-SiO_2, nano-S_8, $K_5CoW_{12}O_{40}$, montmorillonite K-10 clay, trityl chloride, cation exchange resin, deep eutectic solvents and Bronsted acidic ionic liquids.

Conventionally, quinoxalines can be synthesized by direct thermal condensation reaction between a 1,2-dicarbonyl compound and o-phenylene diamine. Apart from these classical approaches, many other methods have also been developed for the oxidative cyclisation of alpha-hydroxy ketones or alpha-halide ketones with 1,2-diamines.

3. Objectives:

The objectives of research proposal are as:

- Development of solvent-free green methodology for synthesis of organic compound using green catalyst.
- Development of catalyst-free green methodology for synthesis of organic compound using green solvent
- Synthesis of biological active organic compounds such benzoazoles, benzofurans, nitriles, amido-alkyl naphthol, quinoxalines, coumarins, chalcones and flavones.
- To characterized the synthesized compounds by spectroscopy techniques IR, NMR, CMR and Mass spectroscopy.

4. Methodology:

All reagents and chemicals will be obtained from commercial suppliers. The physical constant of synthesized compounds will be determined in open capillary tube. The completion of reaction will be confirmed by thin layer chromatography. The crude products will be purified and separated by column chromatography, and preparative chromatography. The spectroscopic techniques such as IR, NMR, CMR and Mass spectroscopy will be used for structure determination of products. The green nano-catalyst used in synthesis can be characterized by UV-visible spectra, SEM, TEM and XRD. All the compounds in proposed work synthesized by using the either the green catalysts or green solvents.

5. Importance of study:

- **International status**

In recent years various research groups have been working on synthesis of bioactive heterocyclic compounds such as azoles, quinoxalines, oxadiazoles, benzoazoles and derivatives. Quinoxalines, benzoxazoles, benzothiazoles, and benzimidazoles are important fragments in

medicinal chemistry because of their wide range of biological activities. For example, mibefradil developed by Merck healthcare, contains a benzimidazole core and is active against hypertension. Zopalrestat, a good representative benzothiazole contain drugs, is used for treatment of diabetic complications and is commercialized by Takeda Pharmaceutical Co. Calcimycin, a benzoxazole derivative produced by combinatorx, is employed as an ionophore antibiotic. Most of the marketed antihypertensive agents such as Tiodazosin and Nesapidil as well as antibiotics such as furamizole contain oxadiazoles nucleus. Cancer is a major human health problem worldwide and is the second leading cause of death in United States.

- **National Status**

As far as our country is concerned, now our India is second largest population country in the world and progressing in research field. We have enough pharmaceutical companies but still we are lagging to get Medical Facilities with low cost. To improve this status, we must use green chemistry approach for organic synthesis to increase yield, decrease the cost of production and environmental pollution. The bioactive heterocyclic compounds which are present in drug are will be synthesized by green chemistry approach which has more yields with low productioncost. Definitely it will help to nation with many points of view.

6. Proposed work Plan:

Sr. No	Duration of work	Plane of work
1	1st, Year	**Literature Survey and References**
2	2nd Year	**Scheme – 1,** The catalyst-free or solvent- free synthesis of substituted benzoazoles using green solvent or green catalyst. **Scheme-2,** The catalyst-free or solvent-free synthesis of 1-amidoalkyl-2napthols using green solvent or green catalyst.
		Scheme-3, Green and one pot protocol for the synthesis of substituted quinoxaline from 1,3-dicarbonyl compounds and

3	**3rd, Year**	1,2-diammine. **Scheme-4,** Green and one pot protocol for the synthesis of 2-aminothiazole from 1,3-dicarbonyl compounds and thiourea.
4	**4th, Year**	**Thesis Writing and Binding**

7. Expected Outcome:

1. Infectious diseases are one of the leading causes of death worldwide. During the past few decades new infectious diseases have appeared and old ones previously thought to be controlled have reemerged. Despite the critical need for new antimicrobial agents, the development of these agents is decline.
2. Among the heterocyclic compound's quinoxalines, oxadiazoles, thiazoles and benzothiazoles has become an important construction motif for the development of new drugs.
3. Heterocyclic compounds and its derivatives show wide spectrum of chemotherapeutic and microbial activity including anti-bacterial, ant-fungal, anti-inflammatory, anti-viral, anti-cancer, anti-hypertensive, analgesic, anti-convulsant and anti-diabetic properties.
4. The ability of heterocyclic compounds to undergo various chemical reactions has made them important for molecules planning because of their privileged structure, which has enormous biological potential.
5. The literature survey indicates that these heterocyclic compounds are synthesized by using different synthetic methods. But these methods are not environmentally and economically beneficial because low yield, use of toxic reagents and solvents. Therefore, there is need to design novel synthetic methodology which avoid these problems.

8. References:

1) P. T. Anastas and J. C. Warner, Green Chemistry: Theory and Practice, Oxford University Press, Oxford, **1998**; / 2005 edition.

2) R. Sheldon, *Nature*, **1999**, 399, 636-637.

3) K. Tanaka and F. Toda, *Chem. Rev.*, **2000**, 100, 1025-1074.

4) R. A. Sheldon and I. W. C. E. Arends, U. Hanefeld, Green Chemistry and Catalysis, Wiley-VCH, Weinheim, **2007**.

5) Green Chemistry Education: Changing the Course of Chemistry (Eds.: P. T. Anastas, I. J. Levy and K. E. Parent), ACS Symposium Series, Vol. 1011, American Chemical Society,

USA, 2009.

6) J. H. Clark, R. Luque and A. S. Matharu, *Annu. Rev. Chem. Biomol. Eng*., **2012**.

7) A. Farrán, C. Cai, M. Sandoval, Y. Xu, J. Liu, M. J. Hernáiz, R. J. Linhardt, *Chem. Rev*., **2015**, 115, 6811-6853.

8) K. Kaneda, T. Mizugaki, *Energy Environ. Sci*., **2009,** 2, 655-673.

9) W. Zhang, *Green Chem*. **2009**, 11, 911-920.

10) N. R. Candeias, L. s. C. Branco, P. M. P. Gois, C. A. M. Afonso and A. F. Trindade, *Chem. Rev*., **2009,** 109, 2703-2802.

11) B. M. Trost, *Acc. Chem. Res*., **2002**, 35, 695-705.

12) R. Sheldon, *Nature*, **1999**, 399, 636-637.

13) M. Sankar, N. Dimitratos, P. J. Miedziak, P. P. Wells, C. J. Kiely and G. J. Hutchings, *Chem. Soc. Rev*., **2012**, 41, 8099-8139.

14) M. Kidwai and P. Mothsra, *Indian J. Chem*., **2006**, 45B, 2330-233

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